REMARKS

I. Specification

Applicants amended the Table bridging pages 20 and 21 by deleting the first column. Applicants do not believe that the column was in any way ambiguous; it simply served to denote discreet samples that Applicants tested. Hence, "Samples" 1 and 2 for normal brain tissue were originally denoted in the first left-most column as entry "1." The next duplicate set of samples, i.e., Samples 1 and 2 for glioblastoma multiforme of the brain, were collectively denoted as entry "2." Likewise, the third batch of biological samples were duplicate tissues of normal breast tissue, e.g., Samples 1 and 2 of normal breast; and so on. Applicants believe that the remaining "Sample," "Tissue," "Diagnosis," and "Age/Sex" columns are self-explanatory and therefore assert that the Table is not ambiguous.

The Examiner also objected to page 6, paragraph 22 of the specification, asserting that it failed to comply with the requirements of 37 C.F.R. § 1.821-1.825. Applicants respectfully direct the Examiner's attention to the Preliminary Amendment filed on November 3, 2004. There, Applicants amended paragraph 22 to reference SEQ ID NO: 5. For convenience, Applicants have reproduced those paragraph 22 amendments on page 2 of this paper.

II. Drawings

The Examiner objected to the drawings as failing to comply with 37 C.F.R. § 1.84(p)(5). Office action at page 3. Applicants provide herewith clearer and cleaner copies of the drawings for the Examiner's review and to place them better form for allowance. In this regard, the photographs of the figures are identical to those originally filed and are presented herein as cleaner, crisper copies for the Examiner's ease of review. Applicants intend to file clean black and white copies of the new formal drawings but also submit, to aid the Examiner's review, courtesy colour copies.

III. Status of the Claims

Claims 1-25 have been examined. Claims 1, 6, 15, 18, 19, and 20 have been amended. Claims 16 and 17 have been canceled without prejudice or disclaimer. Applicants reserve the right to file one or more continuing applications to any canceled subject matter. Claims 26-62 remain withdrawn.

The undersigned thanks Examiner Aeder for taking his telephone enquiry of June 7, 2006, to clarify the status of the claims, and to briefly discuss the enablement rejection and Applicants' proposed amendment in response. In this regard, Applicants do not acquiesce with the Examiner's specific opinion on enablement, but agree at this juncture to amend claim 1 to cover a PAK4/ser-474/colon cancer embodiment, purely to expedite prosecution. Examiner Aeder indicated by telephone that this amendment would be acceptable. Amendments to claims 1, 6, 15, and 18-20 reflect this understanding. Thus, dependent claim 6 is drawn to colon cancer specifically and claims 15-20 clarify that the phosphorylated PAK is PAK4. Claims 16 and 17 are canceled because they were originally drawn to phosphorylation of any PAK protein; hence, they are canceled here simply to ensure consistency with amended claim 1, and not in acquiescence of any position taken by the Office concerning patentability or enablement.

(i) The pending claims are not indefinite

Applicants believe that amended claim 1 moots the rejection of the claims as indefinite under 35 U.S.C. § 112, second paragraph (page 4 of the office action). That is, it is clear from amended claim 1 that the method requires measuring the phosphorylation level of serine-474 on PAK4 and not the total phosphorylation level of all PAK isoforms in the sample.

The Examiner further asks, in consideration of Section 112, second paragraph, whether "an increased level of PAK phosphorylation [would] not be indicative of 'an effect.'" Office action at page 5. Applicants do indeed say in their specification that "an individual who has a level of phosphorylated PAK in a test biopsy that is higher than that normally associated with the tissue from which it was obtained, has an abnormal level of PAK that is potentially treatable with a PAK modulator" (emphasis added; page 11, paragraph 41).

Claim 1, therefore, is drawn to a method that identifies those therapeutic compositions that *lower* an abnormally high level of ser-474-specific PAK4 phosphorylation. Hence, before the individual is given the therapeutic composition, a biopsy sample may record a PAK4 phosphorylation at that residue is "higher" than the phosphorylation level measured in the "subsequent biopsy." Hence, a conclusion, as recited in claim 1, is that the therapeutic composition has the effect of lowering PAK phosphorylation. Thus, Applicants state in the application that such a composition, or "modulator," "preferably decreases PAK activity"

(paragraph 41). Applicants believe that this explanation addresses the Examiner's query but invite him to contact the undersigned by telephone to discuss any further clarification that may be necessary to advance this case toward allowance.

The use of the word "suspect" in claims 7 and 8 implies that the biopsy of claim 1 is from a patient or candidate mammal thought to have a disease or is known to have a disease, such as cancer. There is indeed a nexus between anchorage-independent cell growth and disease. Applicants teach, for instance, that "elevated levels of phosphorylated PAK, especially activated PAK4, correlate well with cells that have an increased propensity to undergo anchorage-independent growth. The latter phenomenon is a mechanism known to be an attributable factor in tumor formation and cancerous growths" (paragraph 41). Accordingly, a biopsy that is "suspected of containing cells capable of anchorage-independent growth" means that the biopsy comes from a mammal that may fall into such a disease category. For at least these reasons, and since claim 1 has been amended in line with the Examiner's position concerning written description, Applicants respectfully request that these rejections be withdrawn.

(ii) The pending claims are enabled for a method for measuring PAK4-specific phosphorylation levels

Claims 1-25 are rejected under 35 U.S.C. § 112, first paragraph, allegedly for lack of enablement. According to the Examiner, the claims are enabled "for a method of monitoring the effect of a therapeutic composition on a mammal that has colon cancer, comprising measuring a first phosphorylation level of PAK4 on ser-474" before and after administration of the therapeutic composition. Office action at page 10. As explained above, Applicants have amended claim 1 and the relevant dependent claims to cover this particular embodied method of Applicants' invention. Accordingly, claims 1-25 are enabled. Applicants therefore respectfully request withdrawal of this rejection.

IV. Conclusion

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment,

to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date June 9, 2006 By V.S. Mohan-Ram

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Amendments to the Drawings:

The drawing sheets attached in connection with the above-identified application containing Figures 1 and 2 are being presented as new formal drawing sheets to be substituted for the previously submitted drawing sheets. The photographs of the figures are identical to those originally filed and are presented herein as cleaner, crisper copies for the Examiner's ease of review. Applicants intend to file clean black and white copies of the new formal drawings but also submit, to aid the Examiner's review, courtesy colour copies.

The specific changes which have been made to Figure 1 are as follows:

The heading of Figure 1 has been amended to delete the "A."

The part depicting "Colon carcinoma in situ/high grade dysplasia" has been designated as 1(a).

The part depicting "Benign epithelium distant from Adenoma" has been designated as 1(b).

The part depicting "Hematoxylin and Eosin stain" has been designated as 1(c).

"FIG. 1" has been amended to "Figure 1".

The specific changes which have been made to Figure 2 are as follows:

The heading of Figure 2 has been amended to delete the "B."

The part depicting "Colon Adenocarcinoma" has been designated as 2(a).

The part depicting "Benign Epithelium" has been designated as 2(b).

The part depicting "Hematoxylin and Eosin stain" has been designated as 2(c).

The heading "C. Section of normal colon from patient (patient details unknown) has been deleted.

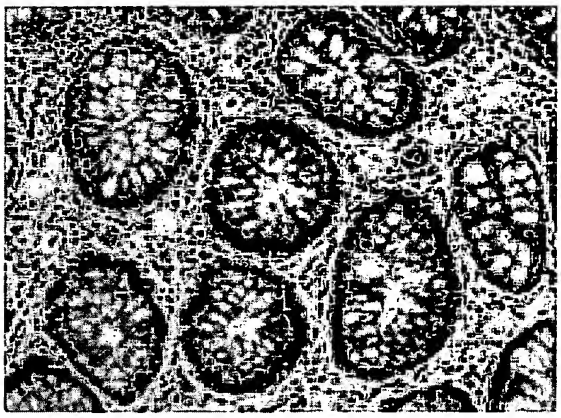
"FIG. 2" has been amended to "Figure 2".

[[A.]]Patient with villous adenoma with high grade adenocarcinoma in situ

Colon carcinoma in situ/high grade dysplasia

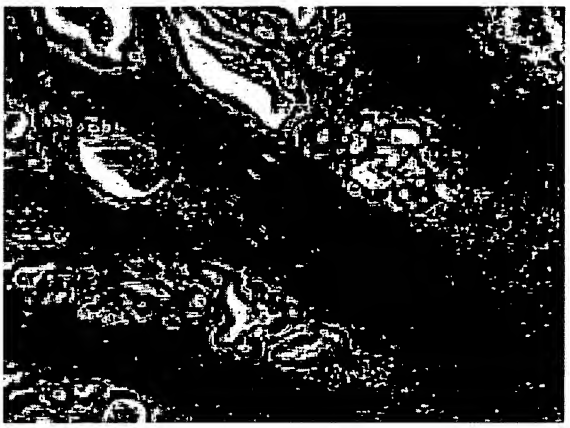
1(a)

Benign epithelium distant from Adenoma



1(b)

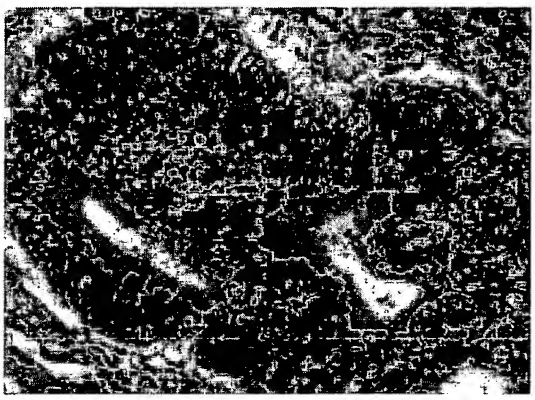
Hematoxylin and Eosin stain



1(c)

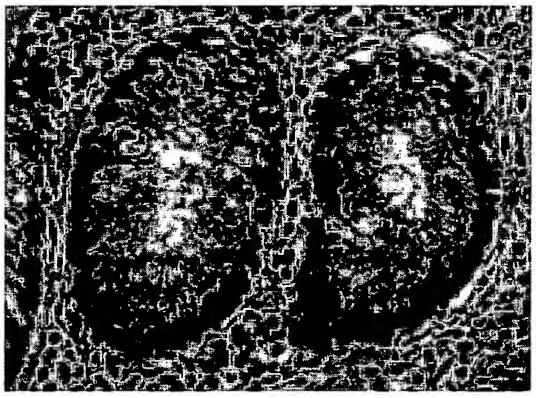
[[FIG. 1]] **Figure 1**

[[B.]] Patient with stage III metastatic adenocarcinoma



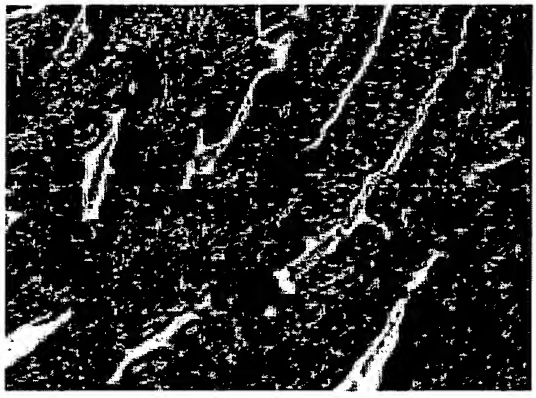
Colon Adenocarcinoma

2(a)



Benign Epithelium

2(b)



Hematoxylin and Eosin stain

2(c)

~~C. Section of normal colon from patient (patient details unknown)~~

[[FIG. 2]] **Figure 2**